IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: TAKAYAMA 10

In re Application of:	Art Unit: 1616
Hiroaki TAKAYAMA, et al.	Examiner: S.N. QAZI
Appln. No.: 10/069,481	Confirmation No. 3430
Date Filed: February 27, 2002	Washington D.C.
For: 2-SUBSTITUTAED VITAMIN D DERIVATIVES	

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner for Patents
Washington, D.C. 20231

I, Hiroaki TAKAYAMA, declare that I am an inventor of the above-identified application and that my current position is Professor of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Teikyo University. I am also a co-author of Suhara et al., *J. Org. Chem* 66 8760-8771, 2001.

My background is as follows:

1957 Graduated from Faculty of Pharmaceutical Sciences, Chiba University

1960 Master's degree in Pharmaceutical Sciences, Tokyo University

1964 Doctorate in Pharmaceutical Sciences, Tokyo University

1965-1966 Post-doctoral research associate at Brown University

1966-1977 Post-doctoral research associate at University of California, Irvine

1961-1977 Research associate and then full-time lecturer of Faculty of Pharmaceutical Sciences, Tokyo University

1977-present Professor of Faculty of Pharmaceutical Sciences, Teikyo University

A combination of Suhara et al., *J. Org. Chem.* 66, 8760-8771, 2001, and Tsugawa et al., *Biol. Pharm. Bull.* 23(1), 2000, can be used to demonstrate that the 2α-vitamin D derivatives of the present invention have much higher VDR binding properties than the 2β-vitamin D derivatives disclosed in Miyamoto et al., U.S. Patent No. 5,877,168.

Test example 1 of the instant application shows that the binding property of the 2α-hydroxypropyl vitamin D derivative (compound 33 of the present invention) is 300, and the VDR binding property of the 2α-ethyl vitamin D derivative (compound 34 of the present invention) is 40.

According to Ono et al., *Chem. Pharm. Bull.* 45(10) at page 1628, Figure 1, and Tsugawa et al., *Pharm. Bull* 23(1):at page 70, Table 2, Code names HAK-3 and AK-2, the binding property of the corresponding 2β-hydroxypropyl compound and the 2β-ethyl compound is 138 and 10, respectively. These values are considerably lower than the values obtained for the vitamin D derivatives of the present invention.

Suhara et al., *J. Org. Chem.* 66, page 8763, compound 9 of Table 1, reported that the binding property of the 2α-butyl compound of the instant invention is 8. According to Tsugawa et al., page 70, code name AK-4, the binding property of the corresponding 2β-butyl compound is 0.9, which is much lower than that of the 2α-butyl compound of the present invention.

It is believed that the VDR binding data of the 2α-vitamin D compounds of Tsugawa et al. are substantially comparable with the data of the instant application, since they were each evaluated as relative values with respect to the same reference compound (1α, 25-dihydroxy vitamin D3), and determined according to substantially the same method based on the same article of Imae et al. (section 2.3, right column, page 303, *Biochim. Biophy. Acta* 1213, 1994).

In the Suhara et al. article, the VDR binding property of the compounds was determined by the same method as in Test example 1 of the instant application. This method is described in Suhara et al. *J. Org. Chem.* 66, at page 8763, lines 8-11 from the bottom, right column. This was the method used in Imae et al. *Biochim. Biophys. Acta* 1213, page 303, 1994, which method is substantially the same as in the instant application. Accordingly, the data shown in Suhara et al. are directly

comparable with the data of the instant application.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 81 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Hiroaki Takayama February 7th, 2003
Hiroaki TAKAYAMA Date

:nmp
G:\BN\Y\YUAS\Takayama10\PTO\takayama 1.132 third declaration.doc